



Evaluation of Inflammatory Markers in Graves' Disease Patients in Orlu, Imo State

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DOI: 10.67224/ioasdjmps.2025.v02i04.007

ABSTRACT	Original Research Article
The study evaluated the Molecular Inflammatory and Immunological markers in Graves' Disease patients in Orlu, Imo State. This work included eighty (80) Graves' Disease patients within the age bracket of 30-60 years old of both gender (males and females), grouped into two (group 1; those without Graves' orbitopathy, GO) and (group 2; those with Graves' orbitopathy). The two groups were of equal sample size of forty (40) study subjects each matched with Age and Gender controls. CRP, IL-23, IFN-gamma, and TNF-alpha, were all measured with different tests kits of Elisa method. However, ESR was measured with Westergren methods. The SPSS statistical computer software (version 21) was used for the analysis. The study showed that ESR, CRP, IL-23, IFN-gamma, TNF-alpha mean serum levels were significantly higher in the two groups when compared to their respective controls ESR mm/hr (32.15 ± 7.08; control as 12.05 ± 4.24), CRP mg/L (20.55 ± 8.98; control as 5.40 ± 2.57) IL-23 pg/ml (37.45 ± 13.63; control as 10.85 ± 5.10), IFN-gamma pg/ml (9.46 ± 5.28; control as 2.85 ± 1.00), TNF-alpha (22.80 ± 4.49; control as 9.10 ± 3.00) for males and (33.23 ± 8.57 ±; control as 13.24 ± 4.64), (21.34 ± 8.24; control as 6.20 ± 2.77), (38.02 ± 13.75; control as 11.48 ± 5.82), (10.05 ± 5.97; control as 3.14 ± 1.08), (23.56 ± 4.85; control as 9.85 ± 3.14) for females. Again, there was a significantly lower mean serum levels of those inflammatory markers in grp 1 than in grp 2; ESR (25.70 ± 3.37; control as 38.60 ± 5.66), CRP (14.20 ± 4.27; control as 26.90 ± 7.91), IL-23 (26.00 ± 2.51; control as 48.90 ± 9.96), IFN-gamma (5.35 ± 0.66; control as 13.57 ± 4.62), TNF-alpha (25.70 ± 3.46; control as 19.90 ± 3.41) for males and (26.45 ± 3.37; control as 13.02 ± 5.65), (14.92 ± 5.01; control as 4.90 ± 2.21), (26.75 ± 2.21; control as 10.03 ± 5.28), (6.15 ± 0.75; control as 2.95 ± 0.98), (26.20 ± 3.57; control as 9.80 ± 3.48) for females. Keywords: inflammatory markers, graves' disease, orlu.	Article History Received: 15-11-2025 Accepted: 23-12-2025 Published: 29-12-2025 Copyright © 2025 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Graves' disease is an autoimmune ailment that primarily impacts the thyroid gland, resulting in hyperthyroidism, characterised by excessive activity of the gland. It is the leading cause of hyperthyroidism worldwide, especially in women aged 30 to 60 years [1].

Clinically, Graves' illness is characterised by a constellation of symptoms including goitre (thyroid enlargement), heat sensitivity, weight loss, palpitations, anxiety, and tremors [2]. Ophthalmopathy, which causes bulging eyes (exophthalmos), redness, and swelling in

about 25% to 50% of those with Graves' disease, is a unique sign of the disease. Dermopathy, including pretibial myxedema, may manifest in certain instances [3].

No one knows for sure what causes Graves' disease, although it is thought to be caused by a mix of hereditary factors and environmental factors like stress, smoking, infections, and maybe even exposure to iodine. A family history of autoimmune illnesses substantially elevates the likelihood of acquiring Graves' disease, suggesting a genetic factor [4].

Antithyroid drugs (such as methimazole), radioactive iodine therapy, and surgery to remove the thyroid gland are all ways to treat Graves' illness. Treatment is usually tailored to each patient based on their age, how bad their sickness is, and whether they have other health problems [5].

It is important to know about Graves' disease's history in order to make a quick diagnosis, teach patients, and treat them well. This is especially true because the condition can have systemic effects and cause long-term problems if not addressed [5].

Autoimmunity is a disorder in which the immune system mistakenly attacks the body's own tissues, causing long-term inflammation and damage to those tissues. The thyroid gland is one of the organs that autoimmune disorders most often affect. Autoimmune thyroid disorders (AITDs), such as Graves' disease and Hashimoto's thyroiditis, are the most common causes of hyperthyroidism and hypothyroidism, respectively [6]. Hashimoto's thyroiditis is characterised by the destruction of thyroid tissue by autoreactive lymphocytes and the presence of antithyroid peroxidase (TPO) and antithyroglobulin antibodies, resulting in a progressive reduction in thyroid function and the onset of hypothyroidism [7]. Both diseases are indicative of a multifaceted interaction including genetic predisposition, environmental stimuli, and immunological dysregulation. Family and twin studies have shown that AITDs have a lot of heritable parts [8]. Environmental factors, including infection, stress, iodine consumption, and smoking, have also been identified as contributing elements [9].

The aetiology of Graves' illness is associated with hereditary and environmental variables; nevertheless, the specific triggers and underlying immunological processes remain unclear [10]. Even while diagnostic technologies and treatment choices have gotten better, there is still a vacuum in understanding. Given the substantial physical, emotional, and financial costs associated with Graves' illness, it is imperative to examine its contributing factors, recurrence patterns, and effective management techniques. More importantly, research is especially needed in underdeveloped areas where people can't easily get specialised treatment and cultural beliefs may affect how people look for health care. If these kinds of things don't happen, the burden of this disease is likely to grow, especially among those who are already at risk. This investigation is relevant and timely due to inconsistent reports and the rising incidence of hyperthyroidism in Nigeria, particularly in Imo State, the study location.

The current study assessed inflammatory markers in patients with different stages of Graves' disease attending the Endocrinology Clinic at Imo State University Teaching Hospital Orlu, Imo State. Graves'

disease may exhibit distinctive inflammatory characteristics shaped by genetic, environmental, or sociodemographic factors particular to the Orlu people. In fact, the way doctors treat patients in the area right now is mostly based on broad treatment guidelines that may not take these local differences into consideration. The lack of localised biomarker evaluation obstructs healthcare practitioners from executing precision medicine strategies that are being promoted in worldwide endocrinologist practice.

Additionally, inflammatory markers including IL-23 and C-reactive protein have been demonstrated to be pivotal in illness development and progression. However, their profiles among patients in Orlu have yet to be examined. This lack of data leads to delays in diagnosis, wrong treatment responses, and a higher disease burden.

Consequently, there is an immediate necessity to assess these indicators within the local community to improve clinical outcomes, inform research-driven treatment strategies, and advance the worldwide comprehension of the disease by insights gained from knowing the people.

Graves' illness has been a big health problem all over the world. Thyroid issues are also one of the most common endocrine diseases that afflict people all over the world.

In general, looking at these inflammatory markers in Orlu will be one aspect of a bigger plan to better understand, diagnose, and treat Graves' illness in Imo State, Nigeria. It connects local health problems with worldwide scientific knowledge and makes it easier for doctors in the community to treat thyroid problems.

MATERIALS AND METHODS

Study Area

This study was conducted at the Imo State University Teaching Hospital (IMSUTH), Orlu, a tertiary healthcare facility located in South-East Nigeria. IMSUTH serves as a major referral centre for the region and provides a wide range of specialist medical services, including internal medicine, endocrinology, immunology, and surgical care. Notably, the hospital offers specialised services in endocrinology and thyroid disorders, including both free and paid thyroid surgeries. These services provided an appropriate clinical platform for the recruitment and management of patients with Graves' disease (GD) and its ocular manifestations.

Study Population

The study population comprised male and female patients diagnosed with Graves' disease within the age range of 30 to 60 years. A total of 80 patients with GD, including those with Graves' orbitopathy (GO) and those without GO, were recruited. In addition, 80 apparently healthy control subjects without Graves'

disease were enrolled for comparison. Targeted random sampling was employed to recruit all eligible and consenting participants.

Selection Criteria

Inclusion Criteria

- Participants were included in the study if they met the following criteria
- Patients with a confirmed diagnosis of Graves' disease based on clinical assessment and clinical activity score (CAS), aged between 30 and 60 years.
- Male or female patients with Graves' disease, either with or without Graves' orbitopathy.
- Patients with Graves' disease who did not have any other metastatic or systemic inflammatory diseases.
- Willingness to participate in the study as evidenced by informed consent.

Exclusion Criteria

Participants were excluded if they met any of the following conditions:

- Individuals younger than 30 years or older than 60 years.
- Individuals from whom informed consent could not be obtained.
- Patients with other metastatic diseases or co-existing systemic conditions that could influence inflammatory markers.

Study Design

This was a case-control, cross-sectional study. A total of 80 patients attending the endocrinology clinic of IMSUTH for the management and surgical treatment of Graves' disease were recruited. The study population consisted of both male and female patients within the specified age range.

Participants were stratified into two major groups:

Group 1: Patients with Graves' disease without Graves' orbitopathy and their age- and sex-matched controls.

Group 2: Patients with Graves' disease with Graves' orbitopathy and their age- and sex-matched controls.

The control group consisted of 80 apparently healthy individuals without Graves' disease. These controls were matched with the study subjects based on age and gender to minimise the confounding effects of these variables on the study outcomes.

Data Collection

A structured and standardised questionnaire was administered to all participants to obtain relevant demographic information and clinical history after informed consent was obtained. Venous blood samples were subsequently collected from all participants for laboratory analysis.

Sample Collection for Graves' Disease Determination

Blood samples were collected from participants using standard venipuncture techniques under aseptic conditions. Portions of the samples were dispensed into clean plain containers and allowed to clot, while others were collected into ethylenediaminetetraacetic acid (EDTA) containers. The clotted blood samples were centrifuged to separate the serum, which was subsequently aliquoted into chemically clean sample bottles. All serum samples were stored frozen at -20°C until laboratory analysis.

Laboratory Procedures

Commercially available diagnostic kits were used for all laboratory analyses, and the manufacturers' standard operating procedures (SOPs) were strictly followed to ensure accuracy and reproducibility of results.

The erythrocyte sedimentation rate (ESR) was determined using the Westergren method. Serum levels of inflammatory markers, including C-reactive protein (CRP), interleukin-23 (IL-23), interferon-gamma (IFN- γ), and tumour necrosis factor-alpha (TNF- α), were measured using enzyme-linked immunosorbent assay (ELISA) techniques.

Ethical Consideration

Ethical approval for the study was obtained from the Ethics Committee of Imo State University Teaching Hospital, Orlu. Written informed consent was obtained from all participants prior to enrolment, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis;

Data obtained from the study was presented in the form of tables, while the results were analysed using SPSS statistical computer software (Version 21). Students T- test, Correlation, mean and standard deviations were determined. The values expressed as mean $\pm$ S.D. The level of significance was set at 95% confidence interval.

RESULT

Table 1: Mean $\pm$ SD Values of Inflammatory Parameters ESR, CRP, IL-23, IFN- γ and TFN- α in Male and Female Hyperthyroidism Subjects Versus Control Subjects.

Variable (mean $\pm$ SD)	Male subjects				Female subjects			
	Hyperthyroidism subjects (n=40)	Control subjects (n=40)	t-value	p-value	Hyperthyroidism subjects (n=40)	Control subjects (n=40)	t-value	p-value
ESR (mm/hr)	32.15 $\pm$ 7.98	12.05 $\pm$ 4.24	14.466	0.000	33.23 $\pm$ 8.57	13.24 $\pm$ 4.64	15.026	0.000
Lower 95% C.I	29.59				30.93			
Upper 95% C.I	34.70	10.69			35.60	11.05		
		13.40				14.10		
CRP (mg/L)	20.55 $\pm$ 8.98	5.40 $\pm$ 2.57	10.440	0.000	21.34 $\pm$ 8.24	6.20 $\pm$ 2.77	10.962	0.000
Lower 95% C.I	17.67				18.76			
Upper 95% C.I	23.42	4.57			23.89	4.98		
		6.22				6.86		
IL-23 (pg/mL)	37.45 $\pm$ 13.63	10.85 $\pm$ 5.10	13.222	0.000	38.02 $\pm$ 13.75	11.48 $\pm$ 5.82	14.242	0.000
Lower 95% C.I					33.98			
Upper 95% C.I	33.08	9.21			42.98	10.24		
	41.81	12.48				13.02		
IFN-γ (pg/mL)	9.46 $\pm$ 5.28	2.85 $\pm$ 1.00	7.591	0.000	10.05 $\pm$ 5.97	3.14 $\pm$ 1.08	7.771	0.000
Lower 95% C.I	7.76				8.65			
Upper 95% C.I	11.15	2.53			12.03	2.96		
		3.16				3.85		
TFN- α (pg/mL)	22.80 $\pm$ 4.49	9.10 $\pm$ 3.00	23.023	0.000	23.56 $\pm$ 4.85	9.85 $\pm$ 3.14	23.983	0.000
Lower 95% C.I	21.36				22.05			
Upper 95% C.I	24.23	8.13			24.97	8.67		
		10.06				10.96		

There was a significantly higher ($p = 0.000$) Mean ESR in Male Hyperthyroidism subjects compared to male control subjects. There was a significantly higher ($p = 0.000$) Mean CRP in Male Hyperthyroidism subjects compared to male control subjects. There was significantly higher ($p = 0.000$) Mean IL-23 of the Male Hyperthyroidism subjects compared to male control subjects. There was significantly higher ($p = 0.000$) Mean IFN- γ in Male Hyperthyroidism subjects compared to male control subjects. There was significantly higher ($p = 0.000$) Mean TFN- α in Male Hyperthyroidism subjects compared to male control subjects. (Table 4.5).

There was a significantly higher ($p = 0.000$) Mean ESR in Female Hyperthyroidism subjects compared to female control subjects. There was a significantly higher ($p = 0.000$) Mean CRP in Female Hyperthyroidism subjects compared to female control subjects. There was significantly higher ($p = 0.000$) Mean IL-23 in Female Hyperthyroidism subjects compared to female control subjects. There was significantly higher ($p = 0.000$) Mean IFN- γ in Female Hyperthyroidism subjects compared to female control subjects. There was significantly higher ($p = 0.000$) Mean TFN- α in Female Hyperthyroidism subjects compared to female control subjects. (Table 1).

Table 2: Mean $\pm$ SD Values of Inflammatory Parameters ESR, CRP, IL-23, IFN- γ and TFN- α in Male and Female Hyperthyroidism Subjects Without Graves Orbitopathy Versus Control Subjects.

Variable (mean $\pm$ SD)	MALE SUBJECTS				FEMALE SUBJECTS			
	Hyperthyroidism Subjects Without G. O. (n=40)	Control subjects (n=40)	t-value	p-value	Hyperthyroidism Subjects Without G. O. (n=40)	Control subjects (n=40)	t-value	p-value
ESR (mm/hr)	25.70 $\pm$ 3.37	12.00 $\pm$ 5.19	9.043	0.000	26.45 $\pm$ 3.37	13.02 $\pm$ 5.65	9.353	0.000
Lower 95% C.I	24.12				24.97			
Upper 95% C.I	27.27	9.57 14.42			28.14	9.86 14.65		
CRP (mg/L)	14.20 $\pm$ 4.27	4.60 $\pm$ 2.21	7.847	0.000	14.92 $\pm$ 5.01	4.90 $\pm$ 2.21	7.937	0.000
Lower 95% C.I	12.19	3.56			13.02	3.87		
Upper 95% C.I	16.20	5.63			17.03	6.03		
IL-23 (pg/mL)	26.00 $\pm$ 2.51	9.90 $\pm$ 5.28	15.504	0.000	26.75 $\pm$ 2.21	10.03 $\pm$ 5.28	15.834	0.000
Lower 95% C.I	24.82	7.42			25.22			
Upper 95% C.I	27.17	12.37			27.97	7.96 12.87		
IFN-γ (pg/mL)	5.35 $\pm$ 0.66	2.88 $\pm$ 0.98	10.537	0.000	6.15 $\pm$ 0.75	2.95 $\pm$ 0.98	10.687	0.000
Lower 95% C.I	5.03	2.42			5.75	2.44		
Upper 95% C.I	5.66	3.33			6.92	3.40		
TFN- α (pg/mL)	25.70 $\pm$ 3.46	9.80 $\pm$ 3.48	28.084	0.000	26.20 $\pm$ 3.57	9.80 $\pm$ 3.48	28.105	0.000
Lower 95% C.I	24.07	8.16			25.34	8.96		
Upper 95% C.I	27.32	11.43			28.45	12.04		

There was a significantly higher ($p = 0.000$) Mean ESR in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to male control subjects. There was a significantly higher ($p = 0.000$) Mean CRP of the Male Hyperthyroidism subjects Without Graves Orbitopathy compared to male control subjects. There was significantly higher ($p = 0.000$) Mean IL-23 in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to male control subjects. There was significantly higher ($p = 0.000$) Mean IFN- γ in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to male control subjects. There was significantly higher ($p = 0.000$) Mean TFN- α in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to male control subjects. (Table 2).

There was a significantly higher ($p = 0.000$) Mean ESR in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to female control subjects. There was a significantly higher ($p = 0.000$) Mean CRP in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to female control subjects. There was significantly higher ($p = 0.000$) Mean IL-23 in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to female control subjects. There was significantly higher ($p = 0.000$) Mean IFN- γ in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to female control subjects. There was significantly higher ($p = 0.000$) Mean TFN- α in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to female control subjects. (Table 2).

Table 3: Mean $\pm$ SD Values of Inflammatory Parameters ESR, CRP, IL-23, IFN- γ and TFN- α in Male and Female Hyperthyroidism Subjects with Graves Orbitopathy Versus Control Subjects.

Variable (mean $\pm$ SD)	MALE SUBJECTS				FEMALE SUBJECTS			
	Hyperthyroidism Subjects With G. O. (n=40)	Control subjects (n=40)	t-value	p-value	Hyperthyroidism Subjects With G. O. (n=40)	Control subjects (n=40)	t-value	p-value
ESR (mm/hr)	38.60 $\pm$ 5.66	12.10 $\pm$ 3.16	23.079	0.000	39.30 $\pm$ 5.74	12.90 $\pm$ 3.74	23.121	0.000
	35.95	10.62						

Lower C.I	95%	41.24	13.57			37.34	11.05		
Upper 95% C.I						41.98	13.95		
CRP (mg/L)		26.90 ± 7.91	6.20 ± 2.70	10.474	0.000	27.03 ± 8.23	6.99 ± 2.90	10.874	0.000
Lower C.I	95%	23.19	4.93				5.05		
Upper 95% C.I		30.60	7.46			23.95	7.85		
IL-23 (pg/mL)		48.90 ± 9.96	11.80 ± 4.87	18.712	0.000	49.62 ± 10.78	12.04 ± 4.98	18.945	0.000
Lower C.I	95%	44.23	9.51				9.96		
Upper 95% C.I		53.56	14.08			45.57	14.84		
IFN-γ (pg/mL)		13.57 ± 4.62	2.82 ± 1.04	9.600	0.000	13.96 ± 4.75	3.21 ± 1.32	9.689	0.000
Lower C.I	95%	11.40	2.33				2.90		
Upper 95% C.I		15.73	3.30			11.90	3.45		
TFN- α (pg/mL)		19.90 ± 3.41	8.40 ± 2.30	14.562	0.000	20.40 ± 3.65	8.89 ± 2.54	14.785	0.000
Lower C.I	95%	18.30	7.32				7.87		
Upper 95% C.I		21.49	9.47			18.90	9.95		
						21.96			

There was a significantly higher ($p = 0.000$) Mean ESR in Male Hyperthyroidism subjects With Graves Orbitopathy compared to male control subjects. There was a significantly higher ($p = 0.000$) Mean CRP in Male Hyperthyroidism subjects With Graves Orbitopathy compared to male control subjects. There was significantly higher ($p = 0.000$) Mean IL-23 in Male Hyperthyroidism subjects With Graves Orbitopathy compared to male control subjects. There was significantly higher ($p = 0.000$) Mean IFN- γ in Male Hyperthyroidism subjects With Graves Orbitopathy compared to male control subjects. There was significantly higher ($p = 0.000$) Mean TFN- α in Male Hyperthyroidism subjects With Graves Orbitopathy compared to male control subjects. (Table 3).

There was a significantly higher ($p = 0.000$) Mean ESR in Female Hyperthyroidism subjects With Graves Orbitopathy compared to female control subjects. There was a significantly higher ($p = 0.000$) Mean CRP in Female Hyperthyroidism subjects With Graves Orbitopathy compared to female control subjects. There was significantly higher ($p = 0.000$) Mean IL-23 in Female Hyperthyroidism subjects With Graves Orbitopathy compared to female control subjects. There was significantly higher ($p = 0.000$) Mean IFN- γ in Female Hyperthyroidism subjects With Graves Orbitopathy compared to female control subjects. There was significantly higher ($p = 0.000$) Mean TFN- α in Female Hyperthyroidism subjects With Graves Orbitopathy compared to female control subjects. (Table 3).

Table 4: Mean ± SD Values of Inflammatory Parameters ESR, CRP, IL-23, IFN- γ and TFN- α in Male and Female Hyperthyroidism Subjects Without Graves Orbitopathy Versus Male and Female Hyperthyroidism Subjects With Graves Orbitopathy.

Variable (mean ± SD)	MALE SUBJECTS				FEMALE SUBJECTS			
	Hyperthyroidism Subjects Without G. O. (n=20)	Hyperthyroidism Subjects With G. O. (n=20)	t-value	p-value	Hyperthyroidism Subjects Without G. O. (n=20)	Hyperthyroidism Subjects With G. O. (n=20)	t-value	p-value
ESR (mm/hr)	25.70 ± 3.37	38.60 ± 5.66	-7.603	0.000	26.10 ± 3.83	39.11 ± 5.83	-7.203	0.000
Lower 95% C.I	24.12	35.95						
Upper 95% C.I	27.27	41.24			24.89	37.05		
CRP (mg/L)	14.20 ± 4.27	26.90 ± 7.91	-6.635	0.000	14.90 ± 4.67	27.30 ± 7.85	-6.135	0.000
Lower 95% C.I	12.19	23.19						
Upper 95% C.I	16.20	30.60						

					12.55		23.01			
					16.85		31.62			
IL-23	26.00 ± 2.51	48.90 ± 9.96	-8.990	0.00	26.84	±	49.90	±	-	0.000
(pg/mL)				0	2.92		10.23		8.010	
Lower 95% C.I	24.82	44.23								
Upper 95% C.I	27.17	53.56			25.03		45.12			
					27.86		53.98			
IFN-γ	5.35 ± 0.66	13.57 ± 4.62	-7.967	0.00	6.35 ± 0.69		13.57	±	-	0.000
(pg/mL)				0			4.62		6.967	
Lower 95% C.I	5.03	11.40			5.21					
Upper 95% C.I	5.66	15.73			6.43		11.94			
							15.98			
TFN- α	25.70 ± 3.46	19.90 ± 3.41	6.250	0.00	26.11	±	20.25	±	6.960	0.000
(pg/mL)				0	3.86		4.05			
Lower 95% C.I	24.07	18.30								
Upper 95% C.I	27.32	21.49			24.80		18.90			
					28.02		22.34			

There was a significantly lower ($p = 0.000$) Mean ESR in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to Male Hyperthyroidism Subjects with Graves Orbitopathy. There was a significantly lower ($p = 0.000$) Mean CRP in the Male Hyperthyroidism subjects Without Graves Orbitopathy compared to Male Hyperthyroidism Subjects with Graves Orbitopathy. There was significantly lower ($p = 0.000$) Mean IL-23 in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to Male Hyperthyroidism Subjects with Graves Orbitopathy. There was significantly lower ($p = 0.000$) Mean IFN- γ in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to Male Hyperthyroidism Subjects with Graves Orbitopathy. There was significantly higher ($p = 0.000$) Mean TFN- α in Male Hyperthyroidism subjects Without Graves Orbitopathy compared to Male Hyperthyroidism Subjects with Graves Orbitopathy. (Table 4).

There was a significantly lower ($p = 0.000$) Mean ESR in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to Female Hyperthyroidism Subjects with Graves Orbitopathy. There was a significantly lower ($p = 0.000$) Mean CRP in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to Female Hyperthyroidism Subjects with Graves Orbitopathy. There was significantly lower ($p = 0.000$) Mean IL-23 in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to Female Hyperthyroidism Subjects with Graves Orbitopathy. There was significantly lower ($p = 0.000$) Mean IFN- γ in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to Female Hyperthyroidism Subjects with Graves Orbitopathy. There was significantly higher ($p = 0.000$) Mean TFN- α in Female Hyperthyroidism subjects Without Graves Orbitopathy compared to Female Hyperthyroidism Subjects with Graves Orbitopathy. (Table 4).

DISCUSSION

This study comprehensively explored the alterations on some molecular inflammatory, in Graves' disease patients, stratified by the presence or absence of Graves' orbitopathy (GO), to uncover the pathophysiological underpinning of pathogenetic activities and Severity of Graves' disease in Orlu, Imo State.

Graves' disease has long transcended its identity as a purely endocrine disorder. In our study, the significantly elevated inflammatory markers; erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), interleukin-23 (IL-23), and immunological markers; interferon-gamma (IFN- γ), and tumor necrosis factor-alpha (TNF- α), strongly reinforce the characterization of Graves' disease as a systemic autoimmune-inflammatory condition rather than a gland-restricted disorder. These biomarkers not only reflect immune system activation but also provide insight into disease progression and severity, with their levels increased progressively in the patients with Graves orbitopathy, which is a more severe stage of the disease [11].

ESR and CRP, although non-specific, are reliable acute-phase reactants that rise in response to systemic inflammation. In this study, both markers were found to be significantly elevated in hyperthyroid patients compared to healthy controls, with the highest levels recorded in the subgroup of patients with Graves' orbitopathy (GO). This stepwise increase with control < hyperthyroid without GO < hyperthyroid with GO, mirrors the intensifying inflammatory burden as the disease progresses from thyroidal involvement to extra-thyroidal manifestations. Notably, elevated CRP and ESR have been observed even in euthyroid phases of Graves' disease, suggesting persistent low-grade inflammation independent of thyroid hormone levels [12]. Their elevation in GO patients likely reflects not only systemic immune activation but also local tissue remodeling and fibroblast proliferation within the orbit.

IL-23, a key cytokine of the Th17 axis, plays a critical role in sustaining pathogenic T helper cells that are implicated in tissue-specific autoimmunity. In this study, IL-23 was markedly elevated in both hyperthyroid groups relative to controls, but significantly more so in the GO subgroup. This elevation suggests that Th17-mediated immune responses may be particularly active in patients with orbital involvement. IL-23 contributes to the recruitment of IL-17-producing T cells, which drive fibroblast activation, glycosaminoglycan production, and tissue edema in GO [13,14]. Thus, IL-23 may serve not only as a diagnostic indicator but as a possible therapeutic target for immunomodulation.

Interferon-gamma (IFN- γ) and tumor necrosis factor-alpha (TNF- α) which are signature cytokines of the Th1 pathway, were also significantly elevated in hyperthyroid patients, with peak values in those with GO [15]. IFN- γ enhances antigen presentation and activates macrophages, while TNF- α amplifies leukocyte trafficking and tissue infiltration. Together, they orchestrate a proinflammatory environment that contributes to both thyroid gland hyperactivity and orbital tissue damage. The greater elevation in GO patients implies a more intense cell-mediated immune response, aligning with findings that Th1-dominant cytokine patterns are associated with active and severe orbitopathy [16, 17]

Interestingly, while most studies support the involvement of these cytokines in Graves' disease and GO, some researchers argue that elevated inflammatory markers may in part result from the systemic metabolic effects of thyroid hormone excess rather than primary immune dysregulation [18,19]. However, the persistence of elevated markers like CRP and IL-23 in patients with normalized thyroid hormones and their association with GO strongly supports an autoimmune mechanism as the dominant driver of inflammation in these patients [20].

Collectively, the progressive increase of ESR, CRP, IL-23, IFN- γ , and TNF- α across the 2 groups; from hyperthyroidism without GO, and finally to highest in hyperthyroidism with GO, not only underscores their diagnostic relevance but also highlights their potential as biomarkers for assessing disease severity, possibly predicting the risk of developing GO and monitoring therapeutic response. These findings support a growing body of literature advocating for the routine assessment of inflammatory markers in the clinical evaluation of Graves' disease, particularly in patients at risk for extrathyroidal complications [21].

The up-regulation of IL-23 and IFN- γ highlights the pivotal role of the Th17/Th1 pathways. IL-23, a cytokine critical for the survival and expansion of Th17 cells, has been implicated in autoimmune tissue remodeling. Elevated IL-23 levels suggest ongoing recruitment and activation of Th17 lymphocytes, which release IL-17, stimulating fibroblast proliferation, pro-

fibrotic signaling, and glycosaminoglycan accumulation in orbital tissues [22]. IFN- γ , secreted by Th1 cells, promotes macrophage activation and enhances antigen presentation, further sustaining autoantigen recognition and tissue damage. TNF- α amplifies both pathways, inducing adhesion molecule expression on endothelial cells and promoting T-cell infiltration into orbital tissues. Collectively, these cytokines are central to the inflammatory cascade that leads to proptosis, diplopia, and fibrosis in GO. Nonetheless, a subset of literature posits that inflammation in GO is largely secondary to thyrotoxicosis-induced oxidative stress, suggesting both endocrine and immune axes driven pathology.

CONCLUSION

This study comprehensively evaluated inflammatory parameters in hyperthyroid patients with and without Graves' orbitopathy (GO) in Orlu, Imo State, with attention to sex-specific differences. The findings revealed that while all hyperthyroid patients shared the classic pattern of elevated nature of associated inflammatory changes differed by sex and GO status.

GO-positive males exhibited a disease profile characterized by higher, IL-23, IFN- γ , NLR and SII suggesting a phenotype dominated by intense autoantibody stimulation and neutrophil-driven inflammation. GO-positive females, in contrast, showed higher TSI, PLR, and MPV, pointing toward a stronger role for platelet-mediated inflammatory mechanisms.

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